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EXAMINER

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Please find below and/or attached an Office communication concerning this application or proceeding.

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Application Number: 08/875,849
Filing Date: September 08, 1997
Appellant(s): BRISKIN ET AL.

MAILED
JUL 06 2007
GROUP 1600

Robert H. Underwood
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 8/16/06 appealing from the Office action mailed 8/15/05.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

This Examiner's Answer is identical to the
Examiner's ~~Answer~~ Answer mailed 11/16/2006
except for the addition of Capow et al. to
Section (8) wherein said reference was already of
record in a pending rejection.

Art Unit: 1644

(2) Related Appeals and Interferences

The following are the related appeals, interferences, and judicial proceedings known to the examiner which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal. An appeal has been filed in related application 08/523004.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is partially correct. The previously pending rejection of claims 24-26, 28-32, 105-108, 111-113, 115, 116, 118-121, 124, 125, 136-150, 152-160 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a

way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention (as per paragraph 4 of the Office action mailed 8/15/05) is withdrawn because all of the pending claims read on fusion proteins containing naturally occurring primate/human MAdCAM or an α 4B7 binding fragment of said naturally occurring primate/human MAdCAM.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

5,599,676	Vonderheide et al.	2-1997
WO 94/13312	Butcher et al.	6-1994
Erle et al., Journal of Immunology, 153:517-528, 1994.		
5,565,335	Capon et al.	10-1996

(9) Grounds of Rejection

(A) Claims 24-26,28-32,105-108,111-113,115,116,118-121,124,125,136-150,152-160 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As per appellants comments, claim 103 was previously cancelled and is therefore not addressed in the instant rejection.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the . . . claimed subject matter", *Vas-Cath, Inc. V. Mahurkar*, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the appellant had possession at the time of invention of the claimed inventions.

The instant claims encompass fusion proteins containing primate MAdCAMs from any primate as well as fusion proteins containing polymorphic or allelic variants of any primate (or human) MAdCAM wherein the proteins have a particular degree of amino acid sequence similarity as per recited in the claims. The specification discloses one amino acid sequence encoding macaque MAdCAM and two different amino acid sequences encoding human MAdCAM. With the exception of the aforementioned disclosed proteins, the skilled artisan cannot envision the detailed structure of the encompassed proteins and therefore conception is not achieved until reduction to

practice has occurred, regardless of the complexity or simplicity of the method of isolation. For example, there is no disclosure in the specification of chimp MAdCAM or baboon MAdCAM or spider monkey MAdCAM or gibbon MAdCAM or rhesus MAdCAM or polymorphic or allelic variants of said primate MAdCAMs. Regarding human MAdCAM proteins and polymorphic or allelic variants of said human MAdCAM protein, there is no disclosure in the specification of human MAdCAM protein other than the two specifically disclosed protein sequences disclosed in the specification. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. In the instant application, the nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

In view of the aforementioned problems regarding description of the claimed invention, the specification does not provide an adequate written description of the invention claimed herein. See *The Regents of the University of California v. Eli Lilly and Company*, 43 USPQ2d 1398, 1404-7 (Fed. Cir. 1997). In *University of California v. Eli Lilly and Co.*, 39 U.S.P.Q.2d 1225 (Fed. Cir. 1995) the inventors claimed a genus of DNA species encoding insulin in different vertebrates or mammals, but had only described a single species of cDNA which encoded rat insulin. The court held that only the nucleic acids species described in the specification (i.e. nucleic acids encoding rat

insulin) met the description requirement and that the inventors were not entitled to a claim encompassing a genus of nucleic acids encoding insulin from other vertebrates, mammals or humans, *id.* at 1240. The Federal Circuit has held that if an inventor is "unable to envision the detailed constitution of a gene so as to distinguish it from other materials. . .conception has not been achieved until reduction to practice has occurred", *Amgen, Inc. v. Chugai Pharmaceutical Co, Ltd.*, 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991). Attention is also directed to the decision of *The Regents of the University of California v. Eli Lilly and Company* (CAFC, July 1997) wherein is stated:

"The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.").

Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA." See *Fiers*, 984 F.2d at 1171, 25 USPQ2d at 1606.

(B) Claims 24-26,28-31,105-108,111,113,115,116,118,120-121,124,126-142,144-147,149-150,152,154,155,157-160 are rejected under 35 U.S.C. 103(a) as being unpatentable over Butcher et al. (WO 94/13312) in view of Vonderheide et al. (US Patent 5,599,676) and Erle et al.

Butcher et al. teach MAdCAM/Ig constant region fusion proteins (see page 7). Murine MAdCAM has an $\alpha 4\beta 7$ integrin-binding fragment. Butcher et al. teach that the peptide is joined to IgG, indicating that the c-terminal of said peptide is joined to the N-terminal of Ig (see page 7). Butcher et al. teach soluble MAdCAM (page 5) and fusion molecules containing said peptide (see page 7). The MAdCAM/Ig fusion protein taught by Butcher et al. contains at least a portion of Ig heavy chain constant region (eg. intact IgG, see page 7). IgG contains hinge, CH2 and CH3 domains because these regions are found in IgG. The fusion protein taught by Butcher et al. is a "hybrid immunoglobulin". Butcher et al. do not teach primate or human MAdCAM fusion proteins. Erle et al. teach that human MAdCAM binds to $\alpha 4\beta 7$ (see abstract). Erle et al. also teach a source of human MAdCAM nucleic acids (eg. they teach that MAdCAM is found in mucosal lymphoid organ HEV and gut lamina propria venules, see page 518, column 1, first paragraph). Erle et al. teach human cell lines expressing $\alpha 4\beta 7$ and MAdCAM (see Abstract). Vonderheide et al. teach methods to isolate nucleic acids encoding molecules that bind $\alpha 4\beta 7$ (see columns 4-10 and claims) wherein said methods require human cell lines expressing $\alpha 4\beta 7$ and human cells expressing

MAdCAM (see Abstract). Vonderheide et al. teach nucleic acids encoding molecules that bind $\alpha 4\beta 7$. Vonderheide et al. teach that such nucleic acids can be used to produce the protein encoded by said nucleic acids (see columns 8-12). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Butcher et al. teach MAdCAM/Ig constant region fusion proteins whilst Vonderheide et al. and Erle et al. provide the means to produce human/primate MAdCAM protein. One of ordinary skill in the art would have been motivated to do the aforementioned because Butcher et al. teach MAdCAM fusion proteins that bind $\alpha 4\beta 7$ could have been used for a variety of art recognized purposes (see abstract).

The art recognizes that multiple alleles of a particular protein commonly exist. For example, a search of WEST indicates that the term allele occurs in 2612 patents filed before the year 1995.

(C) Claims 32,112,119,125,143,148,153,156 rejected under 35 U.S.C. 103(a) as being unpatentable over Butcher et al. (W0 94/13312) in view of Vonderheide et al. (US Patent 5,599,676) and Erle et al. as applied to claims 24-26,28-31,105-108,111,113,115,116,118,120-121,124,126-142,144-147,149-150,152,154,155,157-160 above, and further in view of Capon et al. (US Patent 5,565,335).

The previous rejection renders obvious the claimed invention except that the Ig fusion protein is a homodimer. Capon et al. teach Ig fusion protein homodimers (see claim 8). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the previous rejection renders obvious the claimed invention except that the Ig fusion protein is a homodimer, whilst Capon et al. teach Ig fusion protein heterodimers. One of ordinary skill in the art would have been motivated to do so because homodimeric fusion proteins have a variety of art recognized uses (eg. could be used in immunoassays, etc.).

(10) Response to Argument

(A) Claims 24-26,28-32,105-108,111-113,115,116,118-121,124,125,136-150,152-160 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the

inventor had possession at that time of the . . . claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the appellant had possession at the time of invention of the claimed inventions.

Regarding appellants comments about Example 14 from the Application of Guidelines, said Example deals with a specific claim that recites 95% identity to a particular recited sequence. None of the claims under consideration recite 95% identity to a particular recited sequence and therefore said Example is not germane to the claims under consideration. The instant claims encompass fusion proteins containing primate MAdCAMs from any primate as well as polymorphic or allelic variants of any primate MAdCAM wherein the proteins have a particular degree of amino acid sequence similarity as per recited in the claims. The specification discloses one amino acid sequence encoding macaque MAdCAM and two different amino acid sequences encoding human MAdCAM. With the exception of the aforementioned disclosed amino acid sequences, the skilled artisan cannot envision the detailed structure of the encompassed proteins (or fusion proteins containing said protein) and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. For example, there is no disclosure in the specification of chimp MAdCAM or baboon MAdCAM or spider monkey MAdCAM or

gibbon MAdCAM or rhesus MAdCAM or polymorphic or allelic variants of said primate MAdCAMs. Regarding human MAdCAM and polymorphic or allelic variants of said human MAdCAM, there is no disclosure in the specification of human MAdCAM other than that specifically encoded by the two specific amino acid sequences disclosed in the specification. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. In the instant application, the amino acid itself or isolated protein is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

With the exception of fusion proteins containing SEQ. ID. NO:2 or 4 or 6, there is no disclosure of the amino acid sequences of other primates or primate polymorphic or allelic variants. Said sequences include two sequences derived from human and one sequence derived from a single species of macaque. According to WWW.blarg.com (found by searching Anthroidea on DOGPIL search engine), there are 11 families, 52 genera and 181 species encompassed by the term primate. Thus, appellant has not provided a description of the vast majority (eg. 179 of 181) of the amino acid sequences which encode primate MAdCAM. Furthermore, this figure does not even take into account naturally occurring polymorphic or allelic variants. If each species had multiple alleles or polymorphic variants than the potential number of MAdCAM sequences would vastly increase from the 181 sequences number. There is no

disclosure in the specification of amino acid sequences encoding MAdCAM derived from the primates tufted ear marmoset, mantled howler, brown headed spider monkey, dusky titi, the patas monkey, savanna baboon, haunman langur, the black han gibbon, the bonobo, etc. Applicants disclosure is a minuscule fragment of the potential MAdCAMs derived from species encompassed by the term primate. Regarding appellants comments about claims that recite 75% similar, etc., in view of the fact that said claims do not specify what particular regions of the sequence are similar and do not specify the identity of the nonsimilar portion, it is unclear as to how this provides a further description of the sequence encoding other primate variants. There is also no disclosure in the specification as to how many of the known primate sequences would be encompassed by the percent similarity language recited in the claims.

Regarding appellants comments about the specification, pages 17-22, the SEQ. IDs. recited in the claims are respectively 406/382/345 amino acids in length. The claims encompass primate MAdCAMS that have about 75% or 90% amino acid sequence similarity to the SEQ. IDs. recited in the claims. Thus, the 406 amino acid sequence could differ from about 102(75%) to about 41(90%) amino acids recited in the claims, the 382 amino acid sequence could differ from about 96(75%) to about 39(90%) amino acids, whilst the 345 amino acid sequence could differ from about 86(75%) to about 35(90%) amino acids. There is no disclosure in the specification as to

what 102 or 96 or 75 amino acids could be changed in the SEQ. IDS. recited in the claims to yield an undisclosed primate MAdCAM. There is no disclosure in the specification as to what 41 or 39 or 35 amino acids could be changed in the SEQ. IDS. recited in the claims to yield a primate MAdCAM. There is no disclosure in the specification as to how many primate MAdCAMs would even be encompassed by the percent sequence identity recited in the claims. Similarly, there no such disclosure as it applies to particular human alleles of MAdCAM (as per claimed via the recited percent sequence identity). Furthermore, the Briskin declaration of 11/19/01 (included in the Evidence appendix) demonstrates that it was unpredictable as to what residues could be substituted in MAdCAM without reducing or eliminating MAdCAM activity in a human MAdCAM molecule (see page 4-7). Said experimental data was not present in the specification as filed. Thus, the Briskin declaration indicates that it would have been unpredictable at the time of filing of the instant application as to what residues would or would not be present in a primate or human MAdCAM allele in the context of the percent sequence identity recited in the claims because it was unpredictable as to what amino acids could be substituted and what substitutions would be tolerated while maintaining MAdCAM activity.

Regarding appellants comments, the US CAFC ruled in In Re Wallach et al. (CAFC 03-1327, available on the CAFC website) that written description for a nucleic acid sequence encoding a protein required a complete intact nucleic acid sequence

encoding said protein or a complete intact amino acid sequence of a protein (from which the nucleic acid sequence could be derived). The court ruled that a partial amino acid sequence in itself (from which nucleic acid information could be derived) was insufficient to provide written description for the claimed nucleic acid. In the instant application, the claims encompass amino acids for which no complete amino acid sequence has been furnished. Regarding appellants comments about the structure of MAdCAM disclosed in the specification, there is no disclosure in the specification as to what particular amino acids can or cannot be substituted wherein the fusion protein would maintain all of the required functions of MAdCAM and there is no disclosure as to what particular amino acids substitutions could be tolerated in any particular section of the sequence with the retention of MAdCAM function.

As the MPEP explains, "disclosure of a partial structure without additional characterization of the product may not be sufficient to evidence possession of the claimed invention." MPEP § 2163. Here, Appellants disclosed two human MAdCAM molecules and a single primate molecule, but no description of the other 179 primate MAdCAM molecules encompassed by the claimed invention. In fact, it is unclear as to how many of said molecules would even be included in view of the functional limitation regarding percent similarity recited in the claims. It is also unclear as to how many MAdCAM alleles exist among the 181 primate MAdCAMs. In *Amgen v. Chugai*, the CAFC expounded:

A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound require that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property because an alleged conception having no more specificity than that is simply a wish to know The identity of any material with that biological property. 927 F.2d at 1206. Without that sequence, however, or with only a partial sequence, those structures cannot be determined and the written description requirement is consequently not met.

(B) Claims 24-26,28-31,105-108,111,113,115,116,118,120-121,124,126-142,144-147,149-150,152,154,155,157-160 are rejected under 35 U.S.C. 103(a) as being unpatentable over Butcher et al. (W0 94/13312) in view of Vonderheide et al. (US Patent 5,599,676) and Erle et al.

Regarding appellants comments about In re Deuel, claims 24-26,28-31,105-109,111,113,115,116,118,120-122,124,136-42,144-147,149-150, 152,154,155,157-160 do not recite specific amino acid sequences (or nucleic acids which encode a specific amino acid sequence recited in said claim). Said claims are drawn to sequences that

would be isolated based on the three known MAdCAM nucleic acid molecules disclosed in the specification. The decision in In re Deuel does not address the obviousness of such claims because claims of the scope of claims 24-26,28-31,105-109,111,113,115,116,118,120-122,124,136-42,144-147,149-150,152,154,155,157-160 were not under consideration (eg. all of the claims under consideration were drawn to a specific nucleic acid sequence or a nucleic acid sequence which encoded a specific amino acid sequence recited in said claims). Regarding appellants comments, Vonderheide et al. teach methods to isolate nucleic acids encoding molecules that bind $\alpha 4\beta 7$ (see columns 4-10 and claims). Erle et al. teach that MAdCAM binds $\alpha 4\beta 7$ (see abstract and page 525, first column). Regarding appellants comments about the MAdCAM experiments in Erle et al., Erle et al. indicate that although their experiments used cells transfected with murine MAdCAM, said experiments provide evidence that $\alpha 4\beta 7$ binds human MAdCAM because Amany disclose integrins recognize ligands across species (see page 525, first column). Erle et al. also teach a source of human MAdCAM nucleic acids (eg. they teach that MAdCAM is found in mucosal lymphoid organ HEV and gut lamina propria venules, see page 518, column 1, first paragraph). The method of Vonderheide et al. (US Patent 5,559,676) is disclosed in claims 1-10 of said patent. Vonderheide et al. (US Patent 5,559,676) is an issued patent and the claims of said patent are presumed enabled. In re Deuel and In re Bell deal with issues

related to the degeneracy of the nucleotides encoding for a particular amino acid sequence and the effect that this has on obtaining a particular DNA clone based on amino acid sequence data. Neither case involved teachings of a structurally similar nucleic acid or use of a method recited in claims of an issued US Patent to isolate said structurally analogous molecule. With regards to appellants comments about In re Deuel 34 USPQ2d 1210(Fed. Cir. 1995), the circumstances of In re Deuel differ from the rejection under consideration. In re Deuel deals with issues related to the degeneracy of the nucleotides encoding for a particular amino acid sequence and the effect that this has on obtaining a particular DNA clone based on amino acid sequence data. The method taught by Vonderheide et al. uses $\alpha 4\beta 7$ binding to clone the pertinent molecule, thus overcoming any need for any amino acid data from the protein to be cloned. Furthermore, even with regards to the circumstances surrounding obviousness of DNA based on knowledge of an amino acid sequence, Ex parte Goldgaber 41 USPQ2d 1173 indicates that regarding the issue of whether a method for isolating a DNA molecule makes said molecule obvious, that each case needs to be evaluated on a case by case basis depending on the particular facts in said application. Regarding appellants comments about hindsight reconstruction, Vonderheide et al. teach methods to isolate nucleic acids encoding molecules that bind $\alpha 4\beta 7$ (see columns 4-10 and claims). The method of Vonderheide et al. (US Patent 5,559,676) is disclosed in claims 1-10 of said patent. Vonderheide et al. (US Patent 5,559,676) is an issued patent and the claims of said patent are presumed enabled.

Butcher et al. teach MAdCAM/Ig constant region fusion proteins (see page 7). Murine MAdCAM has a $\alpha 4\beta 7$ integrin-binding fragment. Butcher et al. teach that the peptide is joined to IgG, indicating that the c-terminal of said peptide is joined to the N-terminal of Ig (see page 7). Butcher et al. teach soluble MAdCAM (page 5) and fusion molecules containing said peptide (see page 7). The MAdCAM/Ig fusion protein taught by Butcher et al. contains at least a portion of Ig heavy chain constant region (eg. intact IgG, see page 7). IgG that contains hinge, CH2 and CH3 domains because these regions are found in IgG. The fusion protein taught by Butcher et al. is a "hybrid immunoglobulin". Butcher et al. do not teach primate or human MAdCAM fusion proteins. Erle et al. teach that human MAdCAM binds to $\alpha 4\beta 7$ (see abstract). Erle et al. also teach a source of human MAdCAM nucleic acids (eg. they teach that MAdCAM is found in mucosal lymphoid organ HEV and gut lamina propria venules, see page 518, column 1, first paragraph). Erle et al. teach human cells expressing $\alpha 4\beta 7$ and MAdCAM (see Abstract). Vonderheide et al. teach methods to isolate nucleic acids encoding molecules that bind $\alpha 4\beta 7$ (see columns 4-10 and claims) wherein said methods require human cell lines expressing $\alpha 4\beta 7$ and human cells expressing MAdCAM (see Abstract). Vonderheide et al. teach nucleic acids encoding molecules that bind $\alpha 4\beta 7$. Vonderheide et al. teach that such nucleic acids can be used to produce the protein encoded by said nucleic acids (see columns 8-12).

Given the specific teachings of Vonderheide et al. and the noted success of Vonderheide et al. in identifying and isolating nucleic acids encoding molecules that bind $\alpha\beta 7$, a person of ordinary skill in the art would have had the requisite reasonable expectation of success in identifying and isolating a nucleic acid encoding the MAdCAM molecule recited in the claims. In re O'Farrell, 853 F.2d 894, 903-04, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). The isolated nucleic acid molecule would have been used to produce the claimed fusion protein.

We disagree with appellants that Bell and Deuel dictate reversal of this aspect of the examiner's rejection. As noted previously, appellants criticize the examiner's rejection as focusing on a method of isolating nucleic acids/ molecules encoded by said nucleic acids, relying upon Bell and Deuel. However, we do not read Bell and Deuel as setting forth a per se rule that so-called methodology cannot be taken into account in determining whether a given compound is obvious under 35 U.S.C. § 103(a). See In re Ochiai, 71 F.3d 1565, 1572, 37 USPQ2d 1127, 1133 (Fed. Cir. 1995) ("reliance on per se rules of obviousness is legally incorrect"). Accord In re Brouwer, 77 F.3d 422, 426, 37 USPQ2d 1663, 1666 (Fed. Cir. 1996). Furthermore, when determining whether a given compound would have been obvious within the meaning of the statute, it has been held that not only must a proper motivation to make the compound be identified but that the prior art relied upon "must provide an enabling disclosure." In re Payne, 606 F.2d 303, 314, 203 USPQ 245, 255 (CCPA 1979): The court stated "that an

enabling disclosure is one that places the claimed invention in the possession of the public and that "an invention is not 'possessed' absent some known or obvious way to make it." *Id.* Once the public was put on notice that human MAdCAM existed as a cell surface receptor in cells by Butcher et al./Erle et al., the method described by Vonderheide et al. placed the claimed molecules in the possession of the public. It cannot be gainsaid that a person of ordinary skill in the art would have been motivated to identify and isolate nucleic acids encoding the claimed MAdCAM at the time of the present invention. Butcher et al. describes the existence of MAdCAM fusion proteins that bind $\alpha 4\beta 7$ which could have been used for a variety of art recognized purposes (for example see abstract). Given this motivation, the question becomes does the prior art enable a person of ordinary skill in this art to identify and isolate the claimed molecules. In view of the comprehensive and specific disclosure of Vonderheide et al., we answer that question in the affirmative.

Appellants' position relies upon reading Bell and Deuel as establishing a per se rule that in determining the obviousness of DNA sequences one cannot rely upon so-called methodology. As explained above, we do not read Bell and Deuel as establishing such a per se rule. As noted above, appellants fault the rejection since the applied references do not show a structurally similar compound and in no way render obvious what the claimed invention was. What this argument misses is that persons of skill in this art understood at the time of this invention from Butcher et al. knew that human

MAdCAM existed. While the public would not know amino acid sequence of fusion proteins encoding MAdCAM, Vonderheide et al. provided a powerful new method of identifying and isolating nucleic acids which could be used to produce the claimed fusion proteins. There is no need in using the method of Vonderheide et al. to have any understanding or knowledge of structurally similar compounds. Once the cDNA encoded desired cell surface receptor protein is identified and isolated per the teachings of Vonderheide et al., the skilled artisan may sequence the cDNA as desired using well known methods. Thus, we do not see that the lack of specific information in the applied references in regard to amino acid or nucleotide sequences leads to the conclusion that the claimed subject matter is nonobvious.

The method described in Vonderheide et al. uses human cells expressing MAdCAM and $\alpha 4\beta 7$ to clone the desired nucleic acid and does not require any amino acid data from the protein of interest to be available. Thus, in this case, an entirely different factual foundation is relied upon to support the conclusion of obviousness than was found in either Bell or Deuel. It is also noted that the appellate reviewing court stated in *Enzo Biochem Inc. v. Calgene Inc.*, 188 F.3d 1362, 1374 n.10, 52 USPQ2d 1129, 1139 n.10 (Fed. Cir. 1999), "In view of the rapid advances of science..., what may be unpredictable at one time may become predictable at a later time." We find this caveat to be particularly apt in this case. Vonderheide et al. provides evidence that workers of ordinary skill in the art at the time of this invention were motivated and

enabled to isolate and identify nucleic acids encoding cell surface proteins present on lymphocyte cell surfaces. Vonderheide et al. successfully used that method to identify nucleic acids encoding cell surface adhesion molecules which bound $\alpha 4\beta 7$. Vonderheide et al. was not relied upon in either Bell or Deuel. In our view, Vonderheide et al. provides evidence as to the rapid advances in this art and establishes that it would have been obvious to one of ordinary skill in the art to identify and isolate nucleic acid sequences encoding adhesion molecules such as MAdCAM at the time of the present invention.

(C) Claims 32,112,119,125,143,148,153,156 rejected under 35 U.S.C. 103(a) as being unpatentable over Butcher et al. (W0 94/13312) in view of Vonderheide et al. (US Patent 5,599,676) and Erle et al. as applied to claims 24-26,28-31,105-108,111,113,115,116,118,120-121,124,126-142,144-147,149-150,152,154,155,157-160 above, and further in view of Capon et al. (US Patent 5,565,335).

Appellants arguments are essentially as addressed above.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Ron Schwadron, Ph.D.

Primary Examiner




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